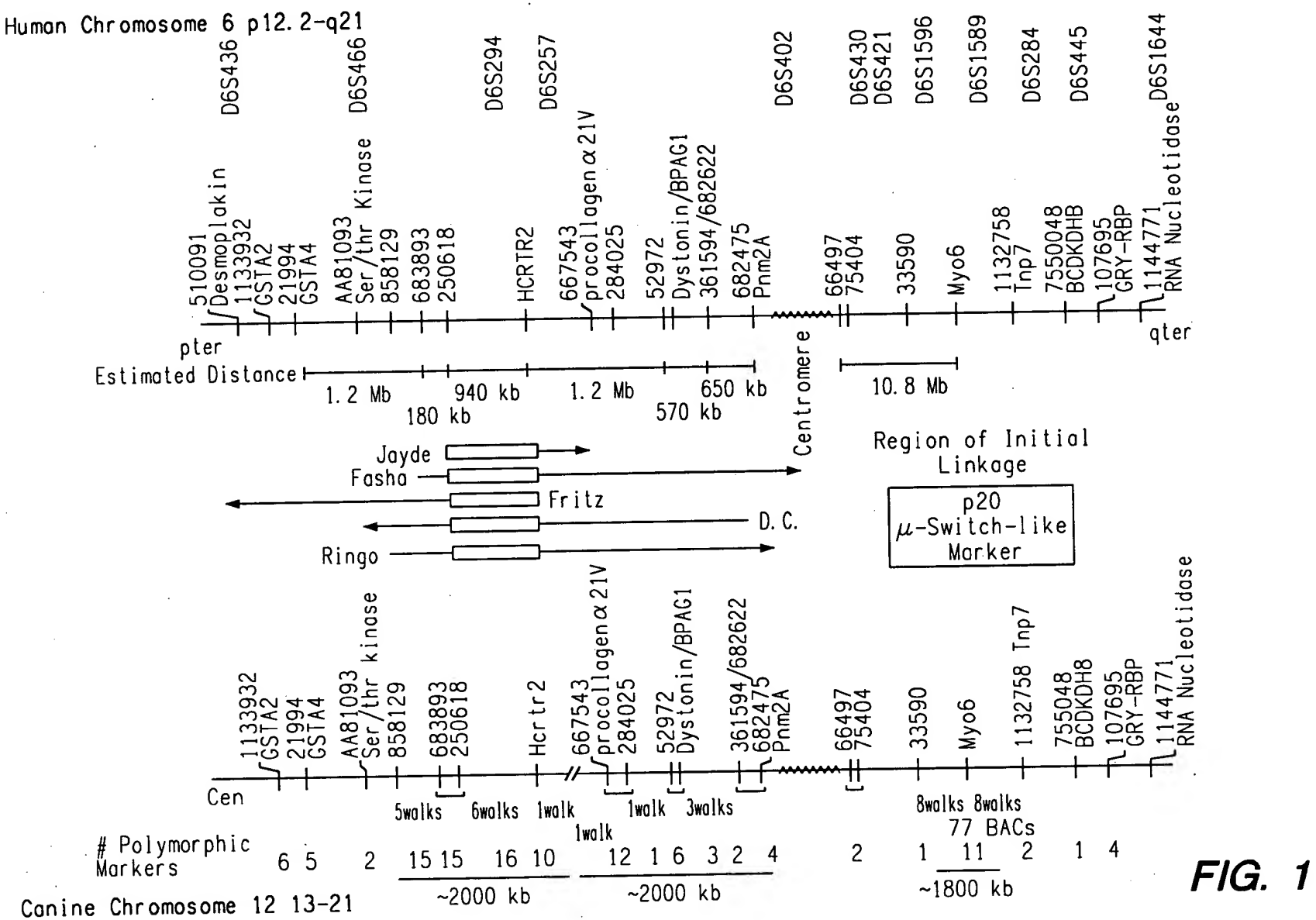
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D6S1644
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21994 GSTA4
AA81093 Ser/thr Kinase
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Fritz
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Ringo
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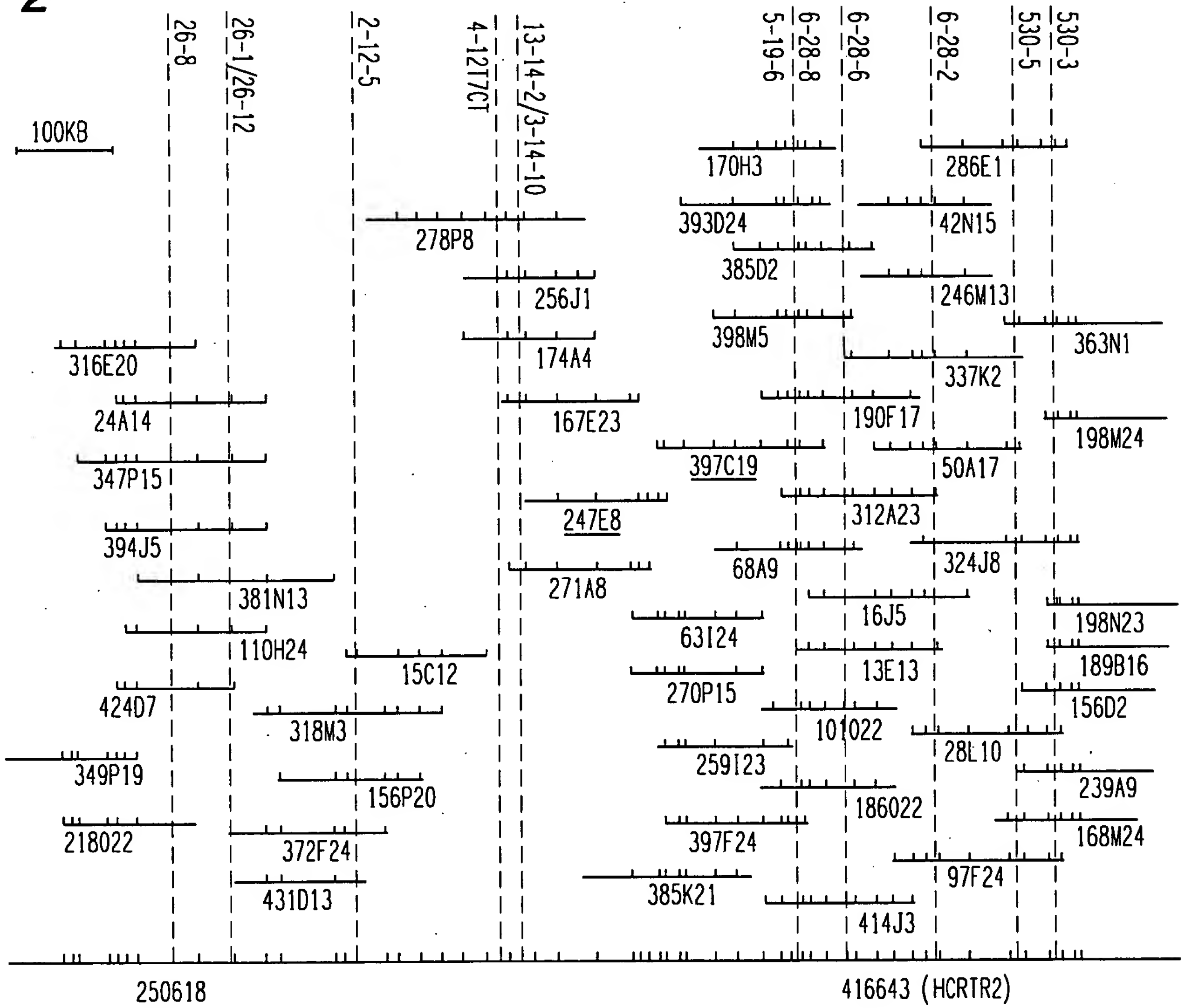
FIG. 1

FIG. 2



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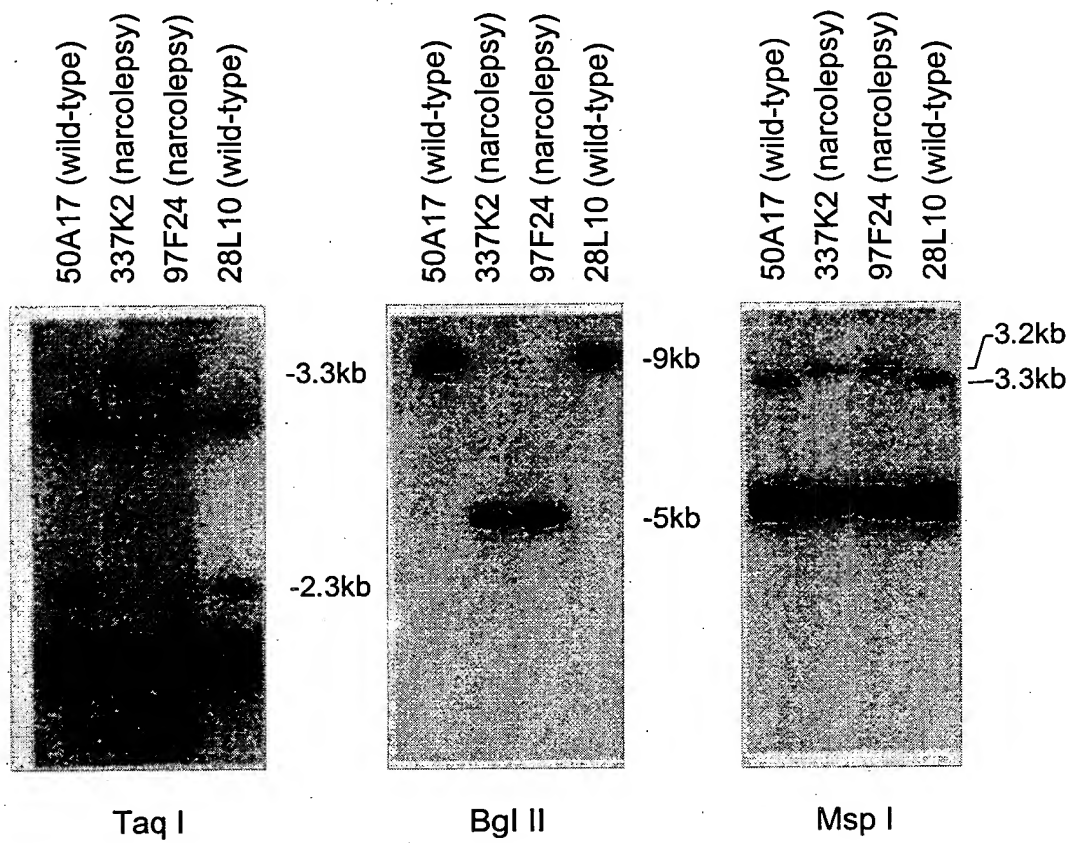

FIG. 3

FIG. 4A

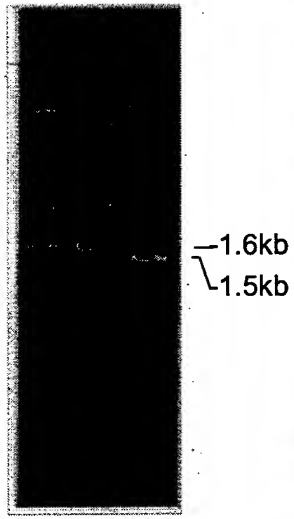

FIG. 4B

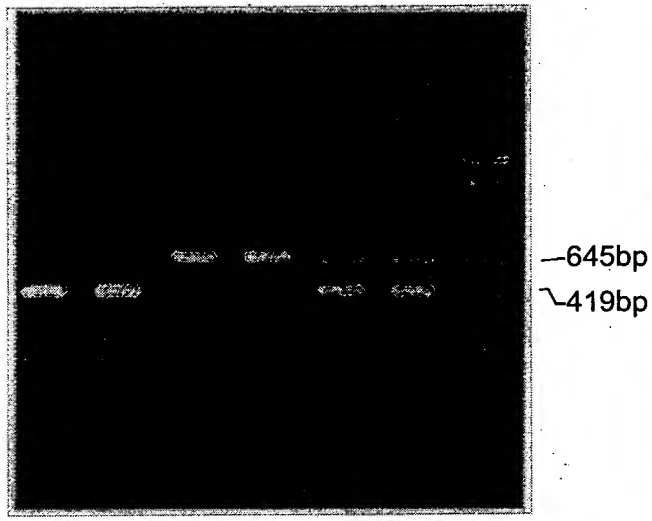

FIG. 4C

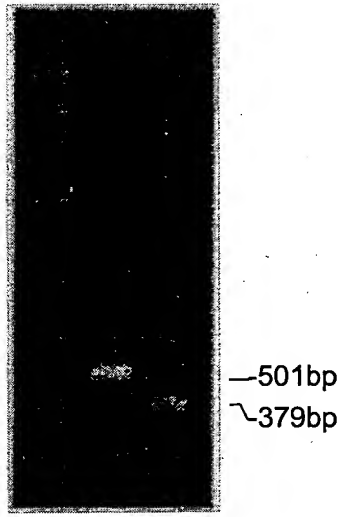

FIG. 5

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Hcrtr2 (dog)          1 MSGTKLEDSPPCRNWSSAPELNETQEPFLNPTDYDDEEFLRYLWREYLHP 50
HCRTR2 (human)        1 MSGTKLEDSPPCRNWSSASELNETQEPFLNPTDYDDEEFLRYLWREYLHP 50
Hcrtr2 (rat)          1 MSSTKLEDSLPRRNWSSASELNETQEPFLNPTDYDDEEFLRYLWREYLEP 50
Hcrtr2 (narc/Lab.)    1 MSGTKLEDSPPCRNWSSAPELNETQEPFLNPTDYDDEEFLRYLWREYLHP 50
Hcrtr2 (narc/Dob.)    1 MSGTKLEDSPPCRNWSSAPELNETQEPFLNPTDYDDEEFLRYLWREYLHP 50

                                ==========TM1======↓=====        =========TM2
Hcrtr2 (dog)         51 KEYEWVLIAGYIIVFVVALVGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD 100
HCRTR2 (human)       51 KEYEWVLIAGYIIVFVVALIGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD 100
Hcrtr2 (rat)         51 KEYEWVLIAGYIIVFVVALIGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD 100
Hcrtr2 (narc/Lab.)   51 KEYEWVLIAGYIIVFVVALVGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD 100
Hcrtr2 (narc/Dob.)   51 KEYEWVLIAGYIIVFVVALVGNVLVCVAVWKNHHMRTVTNYFIVNLSLAD 100

                              ==========                ======↓===TM3==========
Hcrtr2 (dog)        101 VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL 150
HCRTR2 (human)      101 VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL 150
Hcrtr2 (rat)        101 VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL 150
Hcrtr2 (narc/Lab.)  101 VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL 150
Hcrtr2 (narc/Dob.)  101 VLVTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIAL 150
```

FIG. 5 *(continued)*

```
                                  ===========TM4===========
Hcrtr2 (dog)       151 DRWYAICHPLMFKSTAKRARNSIVIIWIVSCIIMIPQAIVMZCSTMLPGL 200
HCRTR2 (human)     151 DRWYAICHPLMFKSTAKRARNSIVIIWIVSCIIMIPQAIVMECSTVFPGL 200
Hcrtr2 (rat)       151 DRWYAICHPLMFKSTAKRARNSIVVIWIVSCIIMIPQAIVMERSSMLPGL 200
Hcrtr2 (narc/Lab.) 151 DRWYAICHPLMFKSTAKRARNSIVIIWIVSCIIMIPQAIVMECSTMLPGL 200
Hcrtr2 (narc/Dob.) 151 DRWYAICHPLMFKSTAKRARNSIVIIWIVSCIIMIPQAIVMBCSTMLPGL 200

                                    ==========TM5==========
Hcrtr2 (dog)       201 ANKTTLFTVCDERWGGEIYPKMYHICFFLVTYMAPLCLMVLAYLQIFRKL 250
HCRTR2 (human)     201 ANKTTLFTVCDERWGGEIYPKMYHICFFLVTYMAPLCLMVLAYLQIFRKL 250
Hcrtr2 (rat)       201 ANKTTLFTVCDERWGGEVYPKMYHICFFLVTYMAPLCLMVLAYLQIFRKL 250
Hcrtr2 (narc/Lab.) 201 ANKTTLFTVCDERWGGEIYPKMYHICFFLVTYMAPLCLMVLAYLQIFRKL 250
Hcrtr2 (narc/Dob.) 201 ANKTTLFTVCDERWGDPWNIICSSEKMEAPAACFTASRARTADQVQD    247
                                                          (SEQ ID NO: 11)

Hcrtr2 (dog)       251 WCRQIPGTSSVVQRKWKPLQPASQPRGPGQQTKSRISAVAAEIKQIRARR 300
HCRTR2 (human)     251 WCRQIPGTSSVVQRKWKPLQPVSQPRGPGQPTKSRMSAVAAEIKQIRARR 300
Hcrtr2 (rat)       251 WCRQIPGTSSVVQRKWKQPQPVSQPRGSGQQSKARISAVAAEIKQIRARR 300
Hcrtr2 (narc/Lab.) 251 WCRQIPGTSSVVQRKWKQLQPASQPRGPGQQTKSRISAVAAEIKQIRARR 300
```

FIG. 5 (continued)

```
                          ==========TM6==========              ========
Hcrtr2 (dog)        301 KTARMLMVVLLVFAICYLPISILNVLKRVFGMFTHTEDRETVYAWFTFSH 350
HCRTR2 (human)      301 KTARMLMVVLLVFAICYLPISILNVLKRVFGMFAHTEDRETVYAWFTFSH 350
Hcrtr2 (rat)        301 KTARMLMVVLLVFAICYLPISILNVLKRVFGMFTHTEDRETVYAWFTFSH 350
Hcrtr2 (narc/Lab.)  301 KTARMLMVVLLVFAICYLPISILNVLKRKV (SEQ ID NO:10)      330

                        ==TM7===========
Hcrtr2 (dog)        351 WLVYANSAANPIIYNFLSGKFREEFKAAFSCCCLGVHHRQEDRLTRGRTS 400
HCRTR2 (human)      351 WLVYANSAANPIIYNFLSGKFREEFKAAFSCCCLGVHHRQEDRLTRGRTS 400
Hcrtr2 (rat)        351 WLVYANSAANPIIYNFLSGKFREEFKAAFSCC-LGVHRRQGDRLARGRTS 399

Hcrtr2 (dog)        401 TESRKSLTTQISNFDNVSKLSEQVVLTSISTLPAANGAGPLQNW (SEQ ID NO:7)
HCRTR2 (human)      401 TESRKSLTTQISNFDNISKLSEQVVLTSISTLPAANGAGPLQNW (SEQ ID NO: 8)
Hcrtr2 (rat)        400 TESRKSLTTQISNFDNVSKLSEHVALTSISTLPAANGAGPLQNWYLQQGV 449

Rcrtr2 (rat)        450 PSSLLSTWLEV                                        460
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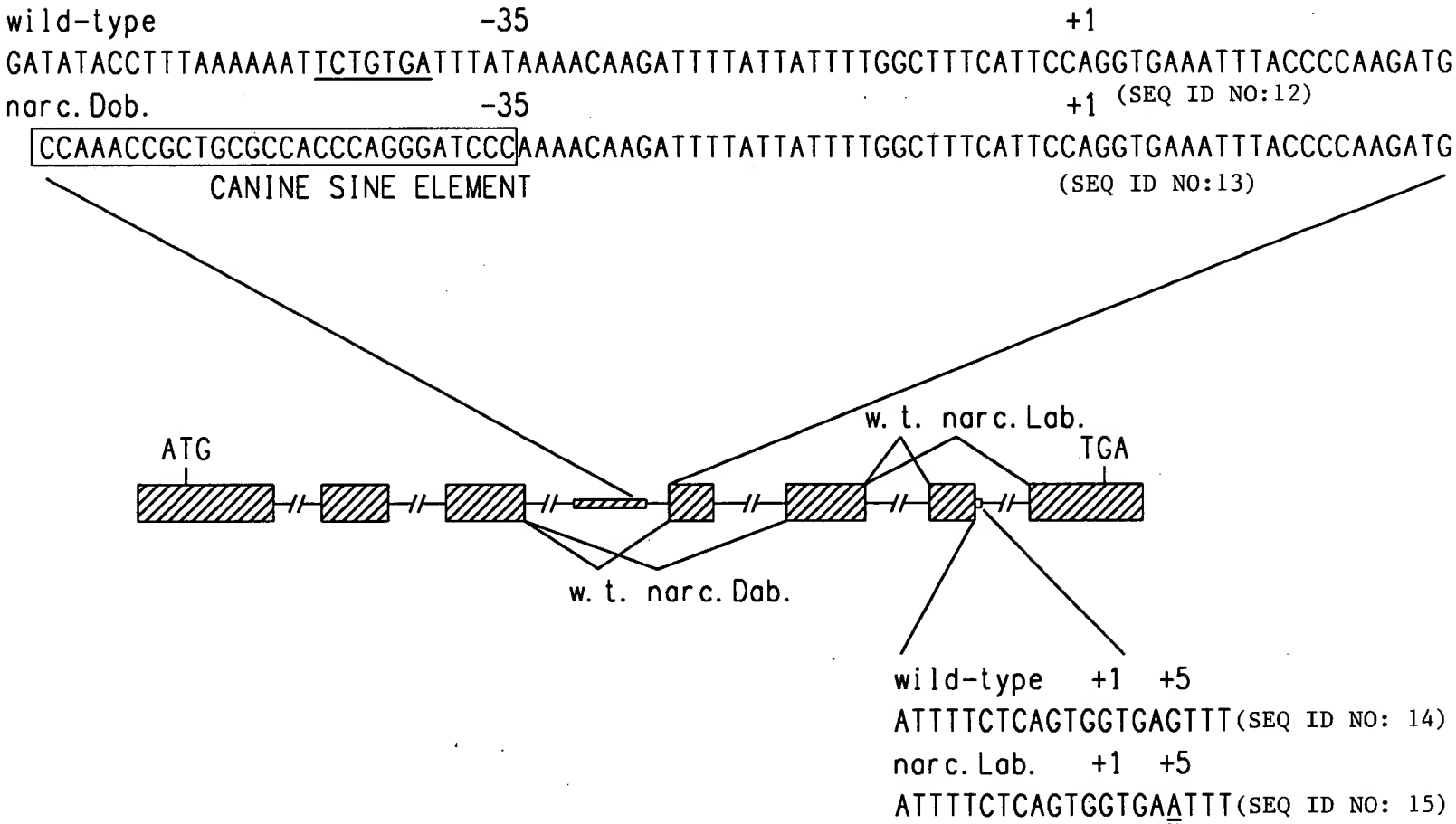
FIG. 6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narc. Dob.
-35
+1
(SEQ ID NO:12)
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CANINE SINE ELEMENT
(SEQ ID NO:13)
ATG
w. t. narc. Lab.
TGA
w. t. narc. Dab.
wild-type +1 +5
ATTTTCTCAGTGGTGAGTTT(SEQ ID NO: 14)
narc. Lab. +1 +5
ATTTTCTCAGTGGTGAATTT(SEQ ID NO: 15)

Fig. 7

HCRT Polymorphisms:

Exon 1

TTGTCTGGCCTGGGTGTGGACGCAAGTGCCTGTCAATTCCCCGCCACCTCA**GAGCACTATAAACCCCAGACCCCTGGGAGTGGG**
TCACAATTGACAGCCTCAAGGTTCCTGGCTTTTTGAACCACCACAGACATCTCCTTTCCCGGCTACCC(C/A)[1]ACCCTGAGCG
CCAGACACCATGAACCTTCCTTCCACAAAGGTAAAGATCCAGGGATGGAGGGGTGACTCACCATCCCAGAGAAGCAAAAA

[1]20 C->A (non coding) (SEQ ID NO: 16)

Exon 2

GGCGGGCGCCGTGGGAAGACCCCCCCAGCGCCCTGTCTCCGTCTCCCTAG**GTCTCCTGGGCCGCCGTGACGCTAC(T/G)[2]GCTG**
CTGCTGCTGCTGCTGCCGCCCGCGCTGTTGTCGTCCGGGGCGGCTGCACAGCCCCTGCCCGACTGCTGTCGTCAAAAGACT
TGCTCTTGCCGCCTCTACGAGCTGCTGCACGGCGCGGGCAATCACGCGGCCGGCATCCTCACGCTGGGCAAGCGGAGGTC
CGGGCCCCCGGGCCTCCAGGGTCGGCTGCAGCGCCTCCTGCAGGCCAGCGGCAACCACGCCGCGGGCATCCTGACCATGG
GCCGCCGCGCAGGCGCAGAGCCAGCGCCGCGCCCCTGCCTCGGGCGCCGCTGTTCCGCCCCGGCCGCCGCCTCCGTCGCG
CCCGGAGGACAGTCCGGGATCTGAGTCGTTCTTCGGGCCCTGTCCTGGCCCAGGCCTCTGCCCTCTGCCCACCCAGCGTCA
GCCCCCAGAAAAAAGGCAATAAAGACGAGTCTCCATTCGTGTGACTGGTCTCTGTTCCTGTGCGGTCGCGTCCTGCCCATCCGG
GGTGGCA

[2]47 T->G (Leu16Arg) (SEQ ID NO: 17)

Fig. 8A

HCRTR1 Polymorphisms:

Exon 1

AATCCCTAATGTTTCCTTCCTTCTCTCTTTTCCCACTCCCTCCTTTCCTTCCTCCCTTCAGGAAGTTTGAGGCTGAGACCCGAAA
AGACCTGGGTGCAAGCCTCCAGGCACCCTGAAGGGAGTGGGCTGAGGGCTGGCCCAAGCTCCCTCCTCTCCCTCTGTAGAG
CCTAGGATGCCCCTCTGCTGCAGCGGCTCCTGAGCTCATGGAGCCCTCAGCCACCCCAGGGGCCCAGATGGGGGTCCCCCC
TGGCAGCAGAGAGCCGTCCCCTGTGCCTCCAGACTATGAAGATGAGTTTCTCCGCTATCTGTGGCG(C/T)[1]GATTATCTGTAC
CCAAAACAGTATGAGTGGGTCCTCATCGCAGCCTATGTGGCTGTGTTCGTCGTGGCCCTGGTGGGCAACACGCTGGGTAGG
TCCAGGGCTTGCCCGGCAGTGCTGCCGGCTTTCCCTGGGGATTGA

[1]111 T->C (synonymous) (SEQ ID NO: 18)

Exon 2

CTAGGATGGGTGTGGCTCTGCCACCAGCTTCACCTCGCTGCACCCTGCAG**TCTGCCTGGCCGTGTGGCGGAACCACCACATGA**
GGACAGTCACCAACTACTTCATTGTCAACCTGTCCCTGGCTGACGTTCTGGTGACTGCTATCTGCCTGCCGGCCAGCCTGCT
GGTGGACATCACTGAGTCCTGGCTGTTCGGCCATGCCCTCTGCAAGGTCATCCCCTATCTACAGGTGAGCTCTGCCCAGGCA
CCCCTCACCACTCCTTGTCACGCCTGTAAAAA (SEQ ID O: 19)

Exon 3

CATCGCTGGGTGGCCCCCAAAATGACCGACGTTGTGTCCCCGTGGGGCAG**GCTGTGTCCGTGTCAGTGGCAGTGCTAACTCTC**
AGCTTCATCGCCCTGGACCGCTGGTATGCCATCTGCCACCCACTATTGTTCAAGAGCACAGCCCGGCGGGCCCGTGGCTCC
ATCCTGGGCATCTGGGCTGTGTCGCTGGCCATCATGGTGCCCCAGGCTGCAGTCATGGAATGCAGCAGTGTGCTGCCTGAG
CTAGCCAACCGCACACGGCTCTTCTCAGTCTGTGATGAACGCTGGGCAGGTAATGGTGGAAGCCTCAAGCAGGCATCCCCTC
AGGTGGGCACTTTGGGA (SEQ ID NO: 20)

Exon 4

GGGTGGGGCTCACGGATTGGGCCTGACTCTGCATCTCTTGACCCCTGCAG**ATGACCTCTATCCCAAGATCTACCACAGTTGCTT**
CTTTATTGTCACCTACCTGGCCCCACTGGGCCTCATGGCCATGGCCTATTTCCAGATATTCCGCAAGCTCTGGGGCCGCCAG
GTGAGGCCCACTCTGGGCAGGGGCTAGGCCAGTCACTGTGTGGGCTGGGG (SEQ ID NO: 21)

Fig. 8B

Exon 5

CACCCTCCCAAGGTGCTGTACCCACCACTGCTGTCTCTATGTGTGCTGGA**CAGATCCCCGGCACCACCTCAGCACTGGTGCGGA**
ACTGGAAGCGCCCCTCAGACCAG(C/A)[2]TGGGGGACCTGGAGCAGGGCCTGAGTGGAGAGCCCCAGCCCCGGGCCC(G/A)[3]C
GCCTTCCTGGCTGAAGTGAAGCAGATGCGTGCACGGAGGAAGACAGCCAAGATGCTGATGGTGGTGCTGCTGGTCTTCGCC
CTCTGCTACCTGCCCATCAGCGTCCTCAATGTCCTTAAGAGGTGAGAGCACGGGGTATGGTTGGGGTGGGGAGAAGTTTGAGG
TTGGGGAAG

[2]793 C->A (Leu265Met); [3]842 G->A (Arg281His) (SEQ ID NO: 22)

Exon 6

CATGCATACGCAGCTACCCCATTTCTGACGCTCCTCCACCCTGGGCCTAG**GGTGTTCGGGATGTTCCGCCAAGCCAGTGACCGC**
GAAGCTGTCTACGCCTGCTTCACCTTCTCCCACTGGCTGGTGTACGCCAACAGCGCTGCCAACCCCATCATCTACAACTTCC
TCAGTGGTGAG(C/T)[4]AGGCTGGGGATGCAAAATGACTGAGGGTGGCCAACAGTCCACAT [4]IVS6 +6C->T (non coding)
(SEQ ID NO: 23)

Exon 7

TCCTGCTGCATCTGTCTCCTTATGGCTGTGTCTTTTGTCTCCCAACCAAG**GCAAATTCCGGGAGCAGTTTAAGGCTGCCTTCTCC**
TGCTGCCTGCCTGGCCTGGGTCCCTGCGGCTCTCTGAAGGCCCCTAGTCCCCGCTCCTCTGCCAGCCACAAGTCCTTGTCC
TTGCAGAGCCGATGCTCC(G/A)[5]TCTCCAAAATCTCTGAGCATGTGGTGCTCACCAGCGTCACCACAGTGCTGCCCTGAGCG
AGGGCTGCCCTGGAGGCTCCGGCTCGGGGGATCTGCCCCTACCCCTCATGGAAAGACAGCTGGATGTGGTGAAAGGCTGT
GGCTTCAGTCCTGGGTTTCTGCCTGTGTGACTCTGGATAAGTCACTTCCT [5]1222 G->A (Val408Ile) (SEQ ID NO: 24)

Fig. 9A

HCRTR2 Polymorphisms:

Exon 1
TCAGCGAGGGAGGAGGCTGTGGGCTGCGGACTGAGTGCTGGAATGAGGA**GTAATTGAGCTTCAGCTGAGCCGGACGTAGCTTT**
CTCCTCCTGGTGTCATTGCTGCAGCCTCCAGTGCCGGGTCCCTAGTTCCTCAGCTGCCTATCTTCCCGGTGCAACATCGCCT
GTAAAGACAGCAAAGCCACCGCAGAAGTTGCCCGGCAGAAGACTCCGGAGGCATTGGCTCAGTAACTTTTCACGTCATTTT
CTGCTCGGGAGCCCCTTCTAGCCTCTCCGCGCAGCCTTTCCCACCGCAAATCACCAGTGCTCATGGGGCAGGCGGAGAGGA
GCTTGCAGCATTGAGCGGAACCGGACTTGAGCCCGTGATGTCCGGCACCAAATTGGAGGACTCC(C/T)[1]CC(C/A)[2]CTTGTCG
CAACTGGTCATCTGCTTCGGAGCTGAATGAAACTCAAGAGCCCTTTTTAAACCCCACCGACTATGACGACGAGGAATTCCTG
CGGTACCTGTGGAGGGAATACCTGCACCCGAAAGAATATGAGTGGGTCCTGATCGCCGGGTACATCATCGTGTTCGTCGTG
GCTCTCATTGGGAACGTCCTGGGTGAGTCTCCTCCCGGGCAGCCCTCCTAGGGGCTATCACCCCCTCTCCG [1]28 C->T
(Pro10Ser); [2]31 C->A (Pro11Thr) (SEQ ID NO: 25)

Exon 2
CAATACCTATTTTCTTTGTTGAGTG(A/C)[3]CTATTCCTTTTTCTTTTCAAATTA**GTTTGTGTGGCAGTGTGGAAGAACCACCACAT**
GAGGACGGTAACCAACTACTTCATAGTCAATCTTTCTCTGGCTGATGTGCTCGTGACCATCACCTGCCTTCCAGCCACACTG
GTCGTGGATATCACTGAGACCTGGTTTTTTGGACAGTCCCTTTGCAAAGTGATTCCTTATCTACAGGTAATTGTTTTTAATGC
TTTTTTGAAGCTACTAAAAAGAATGTTCAGC(C/T)[4]A [3]IVS1 -25A->C (non coding); [4]IVS2 +49C->T (non coding)
(SEQ ID NO: 26)

Exon 3
TCTTTTAACAGCTGGTGCTTCTCTATTACTATGATCTTTCTTTTCTCTAG**ACCGTGTCGGTGTCTGTGTCTGTCCTCACACTGAG**
CTGTATCGCCTTGGATCGGTGGTATGCAATCTGTCACCCTTTGATGTTTAAGAGCACAGCAAAGCGGGCCCGTAACAGCATT
GTCATCATCTGGATTGTCTCCTGCATTATAATGATTCCTCAGGCCATCGTCATGGAG(T/A)[5]GCAGCACCGTGTTCCCAGGCT
TAGCCAATAAAACCACCCTCTTTACGGTGTGTGATGAGCGCTGGGGTGGTAAGTACCTTATGGCCCATCAACTGACATTTATA
TTACAGCAGCAAATT [5]577 T->A (Cys193Ser) (SEQ ID NO: 27)

Exon 4
AAGTCCATCAATTGTAACGTAAGGTTTTGTTGTTTTGACTTTCATCCTAG**GTGAAATTTATCCCAAGATGTACCACATCTGTTTC**
TTTCTGGTGACATACATGGCACCACTGTGTCTCATGGTGTTGGCTTATCTGCAAATATTTCGCAAACTCTGGTGTCGACAGG
TATATAGTTTCAAATATTTTGCGTGCATTATTCCTCCACACATAATTTG (SEQ ID NO: 28)

Fig. 9B

Exon 5
GAACTTTCCTAAGTCAAATTGCAATAAGGGTCTGTCTCTTCTCCTTTCAGATCCCTGGAACATCATCTGTAGTTCAGAGAAAATG
GAAGCCCCTGCAGCCTGTTTCACAGCCTCGAGGGCCAGGACAGCCAACGAAGTCCCGGATGAGCGCTGTGGCGGCTGAAA
TAAAGCAGATCCGAGCCAGAAGGAAAACAGCCCGGATGTTGATG(G/A)[6]TTGTGCTTTTGGTATTTGC(A/G)[7]ATTTGCTATCT
ACCAATTAGCATCCTCAATGTGCTAAAGAGGTAAAACTTATCTGTTATTTGAAAATGAAATAGCCTGCCTTTTCTTGATT [6]922 G->A (Val308Ile); [7]942 A->G (Synonymous) (SEQ ID NO: 29)

Exon 6
TTGAATTTAATTATTTAAAAGACACTTTTCTGTTGTTTCTTTTCCTGCAGAGTATTTGGGATGTTTGCCCATACTGAAGACAGAG
AGACTGTGTATGCCTGGTTTACCTTTTCACACTGGCTTGTATATGCCAATAGTGCTGCGAATCCAATTATTTATAATTTTCTC
AGTGGTGAGTTTTCAACTGTTCTTCCATAAGCCACAATTGTAACCAAGGATGAG (SEQ ID NO: 30)

Exon 7
TGAAGCATTTATGTATAATTCCTTTTCCTTTCATTCTCTCTGTTTGCCAGGAAAATTTCGAGAGGAATTTAAAGCTGCGTTTTCT
TGCTGTTGCCTTGGAGTTCACCATCGCCAGGAGGATCGGCTCACCAGGGGACGAACTAGCA(C/T)[8]AGAGAGCCGGAAGTCC
TTGACCACTCAAATCAGCAACTTTGATAACATATCAAAACTTTCTGAGCAAGTTGTGCTCACTAGCATAAGCACACTCCCAG
CAGCCAATGGAGCAGGACCACTTCAAAACTGGTAGAATATTTATTCATATGACAAGGATACCTGAGTAAAACTATCCTTTTT
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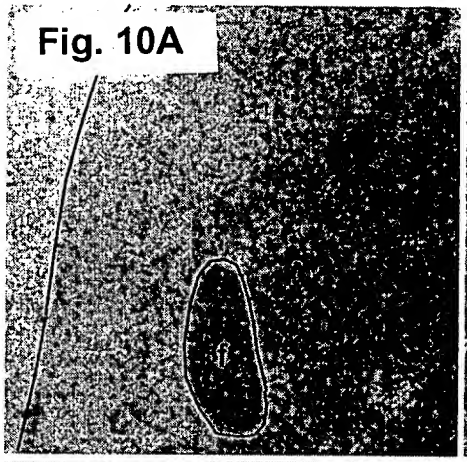
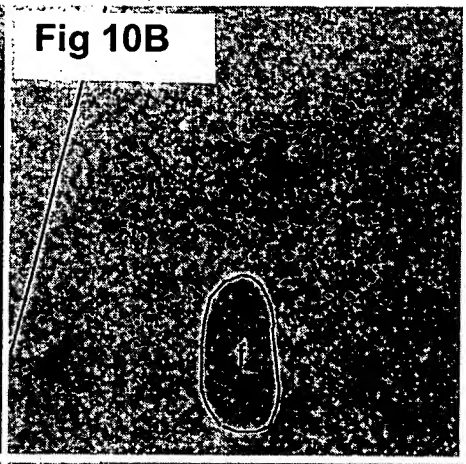
CTCTTTGGAAATAAAAAAAAAGTCAGTTTAAAATGATTTCTCAACTTTTGATTTAAATATGTTAGAAGTTTAACCTTCAATTG
AGCTTATTTCAG [8]1202 C->T (Thr401Ile) (SEQ ID NO: 31)

Narcoleptic

Control

Hypocretin





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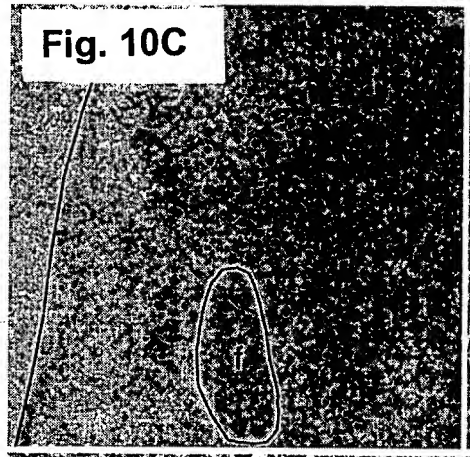

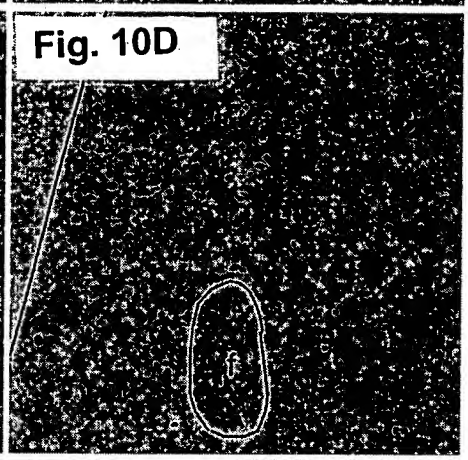

HLA